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DOI: https://doi.org/10.1007/s00701-003-0102-6

A New Subdural Probe for Combined Intracranial Pressure (ICP) and Cerebral Blood Flow (CBF) Monitoring

Technical case report

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Summary

We report the development of a new subdural probe for combined intracranial pressure (ICP) and cerebral blood flow (CBF) monitoring with near infrared spectroscopy (NIRS) and indocyanine green (ICG) dye dilution. For NIRS a conventional subdural ICP monitoring probe was supplied with two fiber bundles and 90-degree prisms. Injections of 25mg ICG were performed. Regional values for the mean transit time of ICG ($rmtt_{ICG}$), cerebral blood flow (rCBF) and cerebral blood volume (rCBV) were calculated. With prototypes of the probe in two patients with intracerebral haemorrhage 18 comparative measurements obtained simultaneously with conventional NIRS (optodes placed on the skin) and the subdural NIRS probe were performed. The new subdural NIRS probe allows combined monitoring of ICP and cerebral hemodynamics in the brain directly, without the influence of extracerebral tissue.

Key words

Cerebral blood flow, indocyanine green dye dilution, intracranial pressure, near infrared spectroscopy

Introduction

New techniques combining near infrared spectroscopy (NIRS) and indocyanine green (ICG) dye dilution to estimate cerebral hemodynamics have been developed [2, 11-13, 16, 20, 26, 27]. Nevertheless, the influence of extracerebral bone and surface tissue on cerebral NIRS signal obtained over the skull has not been clarified yet in the adult head [9, 11, 12, 21, 25]. Most attempts to subtract extracerebral contamination involve spatial resolved spectroscopy (SRS) [9, 19]. Nevertheless, interindividual variability of anatomical structures (bone thickness, extracerebral vasculature, liquor space, etc.) may restrict the reliability of SRS.

The purpose of our investigation was to develop a new subdural probe for combined ICP and CBF monitoring by NIRS and ICG dye dilution. Furthermore a completely new approach to quantify and subtract extracerebral contamination by NIRS optodes placed in the subdural space is to be found.

Method

The study was approved by the Ethics Committee of the University of Zurich (E-020/2000). Measurements were performed in two patients with severe intracerebral haemorrhage (ICH) (Glasgow Coma Scale 3) treated with emergency microsurgical hematoma evacuation.

A conventional subdural probe for ICP monitoring (fluid coupled device) (NMT Neurosciences, Frankfurt, Germany) was supplied with a 2mm thick and 250 mm long NIRS probe consisting of two fiber bundles. Each fiber bundle terminated in a 90-degree prism, one to couple the infrared light into the tissue and one to couple it back into the fibers (distance between the two prisms 35mm).

In two patients with ICH, after evacuation of the hematoma and before complete closing of the dura, the combined subdural ICP-NIRS probe was inserted between dura and cortex placing the tip of the probe over the left frontal lobe (figure 1). In addition to the subdural NIRS probe two NIRS

optodes were placed on the forehead, emitter and detector 5 cm apart (conventional NIRS). ICG (ICG-Pulsion; Pulsion Medical Systems, Munich, Germany) in a dose of 25mg was injected central venous. The appearance of ICG in the optical fields and the dye dilution curves obtained by the subdural NIRS probe and the conventional NIRS probe on the scalp were recorded simultaneously (Oxymon, Artinis Medical Systems, Arnheim, the Netherlands). The spectrophotometer uses three laser diodes at different wavelengths (905, 850 and 770 nm) with a sampling rate of 10 Hz. The ICG concentrations were calculated based on the changes in optical densities (OD). rCBFNIRS was calculated by dividing the regional cerebral blood volume (rCBVNIRS) by the regional mean transit time of ICG (rmttICG) through the examined optical segment.

$$rCBF_{NIRS} = \frac{rCBV_{NIRS}}{rmtt_{ICG}} \tag{1}$$

The mean transit time can be calculated using a “black box“ analysis approach to the dye dilution curve [17]. In principle, the “black box“ approach describes the passage of an indicator through an organ by a convolution integral [17]:

$$o(t) = \int_0^t i(t-u) \cdot g(u) du \tag{2}$$

i(t) is the time course of the indicator concentration at the inflow of the system, o(t) the time course of the indicator concentration at the outflow, and u the integration variable for the convolution procedure. The unit response function g(u), also termed “transport function“ in the context of indicator dilution theory [1], describes the process of indicator dispersion by the organ. Usually, the „transport function“ g(t) cannot be directly obtained in indicator dilution experiments; instead, the total concentration of the indicator in the examined optical segment is recorded. From the total concentration, the concentration time courses at the inlet i(t) and the outlet o(t) of the system can be derived. Hence, the “transport function“ must be computed by nonlinear least-square fitting based on a model assumption for g(t). The approach chosen to model the transport process of ICG through the brain is described in the appendix.

Findings

Prototypes of the probe were inserted in two patients. In these two cases, no complications associated with the insertion of the probe or with the measurement procedure were observed. 9 pairs of simultaneous measurements with conventional NIRS (optodes placed on the scalp) and the subdural NIRS probe were performed. With the NIRS measurements mean values for ICP were 7 mmHg (range 5 – 12 mmHg), for MAP (mean arterial pressure) 89 mmHg (range 80 – 96 mmHg) and for $PaCO_2$ 38 torr (33 – 43 torr). $Rmtt_{ICG}$ values obtained by the subdural probe were lower with a mean value of 9.2 sec compared to those obtained by conventional NIRS with a mean value of 10.2 sec. RCBF and rCBV estimated by conventional NIRS were lower ($rCBF_{mean}$ 16.2 ml/100g/min and $rCBV_{mean}$ 2.4 ml/100g) than the corresponding values obtained by the subdural NIRS probe ($rCBF_{mean}$ 18.5 ml/100g/min and $rCBV_{mean}$ 3.0 ml/100g).

Interpretation

The established methods for bedside measurement of cerebral blood flow (CBF) with inert tracers such as the nitrous oxide dilution method [14] or the 133Xenon dilution technique [22] are technically difficult and time consuming. Stable xenon-enhanced computed tomography, positron emission tomography (PET), single-photon emission computed tomography (SPECT), or perfusion-weighted magnetic resonance spectroscopy require that the patient is transported to the imaging unit, which carries a potential high risk. Therefore, a suitable method for bedside CBF measurement, which is easy to perform and can be repeated rapidly is still a matter of investigation.

New techniques for estimation of $rmtt_{ICG}$, rCBF and rCBV have been developed by combining NIRS and ICG dye dilution [2, 11-13, 16, 20, 26, 27]. Although NIRS seems to reflect significant changes in intracerebral vessels, it has not been demonstrated so far that these changes can be

reliably distinguished from changes in extracerebral tissue [9]. The effects of bone and surface tissue blood flow on NIRS-measurements have been already extensively discussed in modeling studies [23] in oximetry [15] as well as in studies to estimate adult cerebral hemodynamics [5, 11, 21, 25]. There is evidence, that the influence of surface tissues on the NIRS measurements in adults can be reduced by increasing the optode spacing [9, 11, 21, 25]. On the other hand Monte Carlo simulations suggest that with an optode spacing of 5 cm the extracerebral pathlength may represent up to 75% of the total optical pathlength [24].

In our preliminary observations $rmtt_{ICG}$ values obtained by the subdural NIRS probe were lower than those values obtained by conventional NIRS. This corresponds with cerebral angiography showing that the transit time of radiopaque material is longer in the extracerebral vasculature than in the brain vessels. rCBF and rCBV values estimated by NIRS on the scalp were lower than those estimated by subdural NIRS. Hopton and coworkers found CBV values estimated by NIRS and ICG dye dilution to be low in comparison with PET examinations [12]. Owen-Reece and coworkers performed paired measurements from the scalp and the open dura in neurosurgical patients and suggest that the difference in CBV between scalp and dura measurements is likely to be caused by the optical effect of extracerebral tissue, powerfully scattering light [25]. In fact, measured with the intravenous 133Xe technique, blood flow in extracerebral tissue could be estimated to be 5-8 ml/100g/min [8]. From their studies Owen-Reece and coworkers concluded that in NIRS measurements on the scalp, CBF is approximately underestimated by a factor 3 which coincides with the ratio of the optical pathlength in the brain compared with the total pathlength [25].

The new subdural NIRS probe will provide the opportunity to measure directly the concentration of the chromophores in the brain, without the influence of extracerebral tissue. However, there are limitations of the subdural NIRS technique to be considered. The probe must be inserted as far as possible in direct contact to the brain surface. Cerebrospinal fluid (CSF), known to cause light tracking [32], or postsurgical blood collections in the subarachnoid, subdural, or intraparenchymal tissue may interfere with measurements from the subdural space. Illuminated brain tissue thus may

represent an optically heterogeneous compartment of different absorbing components [18]. Larger vessels absorb more light than small vessels [18]. However, as most vessels penetrating the cortex are of small diameter (about 0.04 mm) [12], the distribution of blood in the vessels will have little effect upon the measurement of cerebral hemodynamics [7]. Where changes of the blood volume occur in the larger vessels (>0.2 mm diameter), on the surface of the brain, NIRS may underestimate these variations [7]. Furthermore unpredictable patterns of flow may occur through damaged tissues. Compared to the subdural probes for ICP monitoring, intraventricular catheters have the considerable advantage that they allow treatment of elevated ICP by drainage of cerebrospinal fluid. In future, intraventricular catheters may be supplied by fiberoptic bundles as well.

In conclusion, this technical case report presents the invention of a new subdural probe for combined ICP and CBF monitoring and the application of prototypes in two first patients. To further evaluate whether the new technique is a precise and accurate method of estimating CBF, more repeated measurements and comparisons with a standard method for CBF measurement should be made. Combined monitoring of ICP and NIRS will be of special clinical value in patients with severe stroke, subarachnoid haemorrhage and head trauma, already provided with subdural ICP probes for treatment of intracranial hypertension and being especially at risk for secondary ischemic brain damage. The new subdural NIRS probe gives the opportunity to eliminate extracerebral contamination and will provide some unique physiological information in NIRS technology. To calculate the influence of extracerebral contamination comparative measurements can be performed with conventional NIRS probes on the scalp. Eliminating extracerebral contamination, subdural NIRS methodology may become of major importance as a monitoring technique in the environment of Intensive Care and Stroke Units.

Acknowledgements

The University of Zurich, the Department of Neurosurgery, University of Zurich, the EMDO Stiftung, Zurich, and the Gebert Rüf Stiftung Switzerland financially supported the study. The authors thank Mr. Peter Roth, Department of Neurosurgery University of Zurich for the artificial drawing.

All authors state that they have no personal or institutional financial interest in drugs, materials or devices described in the manuscript.

Appendix

Based on the Fick`s principle the total concentration of the dye at a time t (c(t)) in the examined volume is equal to the integrated difference between the rate of arrival and the rate of departure of the substance [4]:

$$c(t) = \int_0^t i(t) - o(t)dt \qquad \left[c(t) = 0 \ for\ all\ t \le 0\ \right] \tag{3}$$

By deriving both sides of the equation and inserting (2) for o(t) we get

$$\frac{d}{dt}c(t) = i(t) - \int_0^t i(t-u)\cdot g(u)du \tag{4}$$

It is well known that the intravascular transport process g(u) can be adequately modeled by a logarithmic normal density function [10, 29]:

$$g(t) = \frac{1}{\sqrt{2\cdot\pi\cdot\sigma\cdot t}}\cdot e^{-\frac{\left(\ln\frac{t}{rmttNIRS}+\frac{\sigma^2}{2}\right)}{2\cdot\sigma^2}} \tag{5}$$

Since the parameters of the characteristic transport function are known only rmttICG has to be determined by variation until i(t) and o(t) get a reasonable shape. Prerequisite conditions are for example that neither i(t) nor o(t) may be negative at anytime and that i(t) has to be a sum of g(u) - like functions because the initial bolus is recirculating and distributing in the vascular system.

The measured light absorption shows a pulsatility that is correlated with the variability of the arterial blood volume induced by systole and diastole [31]. The amplitude (A(t)) of this pulsatility can be defined as

$$A(t) = A_0(a_{Hb}c_{Hb}(t) + a_{ICG}c_{ICG}(t)) + C \quad (6)$$

A0 and C are measurement specific constants, aHb, aICG are the absorption coefficients of Hb and ICG and cHb, cICG are the concentrations of Hb and ICG in the blood. Specific absorption coefficients of ICG were at 782 nm 113.3 (mmol/L)-1.cm-1 and at 857 nm 17.117 (mmol/L)-1.cm-1. Since cICG is 0 before the injection (t0) and cHb is approximately constant during the measurement, the dye concentration in the blood after the injection is

$$c_{ICG}^{blood}(t) = \left(\frac{A(t)}{A(t_0)} - 1\right)\frac{a_{Hb}c_{Hb}}{a_{ICG}} \quad (7)$$

The modified Lambert-Beer law [3] is given by:

$$OD(t) = adBc(t) + G \quad (8)$$

OD is the optical density of the dye, d the geometrical distance, a the absorption coefficient and c the concentration. B is the differential path length factor and accounts for the increase in optical pathlength due to the scattering in the tissue. An optical pathlength factor of 5.93 is used [30]. G represents the dye independent light losses due to scattering and absorption in the tissue and is constant during the measurement. For more than one chromophore, e.g. hemoglobin and the injected dye ICG, this equation is given by:

$$OD(t) = dB((a_{Hb}c_{Hb}(t) + a_{ICG}c_{ICG}(t)) + G \quad (9)$$

Since cICG is 0 before injection (t0) and cHb remains constant during the measurement, the concentration of the dye after the ICG injection is

$$c_{ICG}^{tissue}(t) = \frac{OD(t) - OD(t_0)}{a_{ICG}dB} \quad (10)$$

If the dye is homogenously distributed in the blood, rCBVNIRS is calculated as the ratio of the concentration of ICG in the illuminated volume of tissue (cICGtissue) measured by NIRS and the concentration of ICG in cerebral blood (cICGblood):

$$rCBV_{NIRS} = \frac{c_{ICG}^{tissue}}{c_{ICG}^{blood}} \tag{11}$$

rCBFNIRS can then be calculated as

$$rCBF_{NIRS} = \frac{rCBV_{NIRS}}{rmtt_{NIRS}} \tag{12}$$

The Fahraeus effect states that the hematocrit (Hct) of blood in the small cerebral vessels is less than in the large vessels because of axial streaming and differing plasma and red cell flow rates [6]. Sakai et al. found with SPECT examinations in healthy volunteers mean regional cerebral Hcts in small vessels to be 75.9 +/- 2.1% of the large-vessel Hct [28]. This is normally referred to as the cerebral-to-large-vessel Hct ratio and is known to vary from one physiological state to another [28]. For estimation of CBVNIRS a mean cerebral-to-large-vessel Hct ratio of 0.75 was taken into account.

Figure legends

Figure 1: **Combined subdural ICP-NIRS probe**

Inserted through a burr hole in the skull, the probe is in direct contact with the brain and elimination of extracranial contamination is gained.

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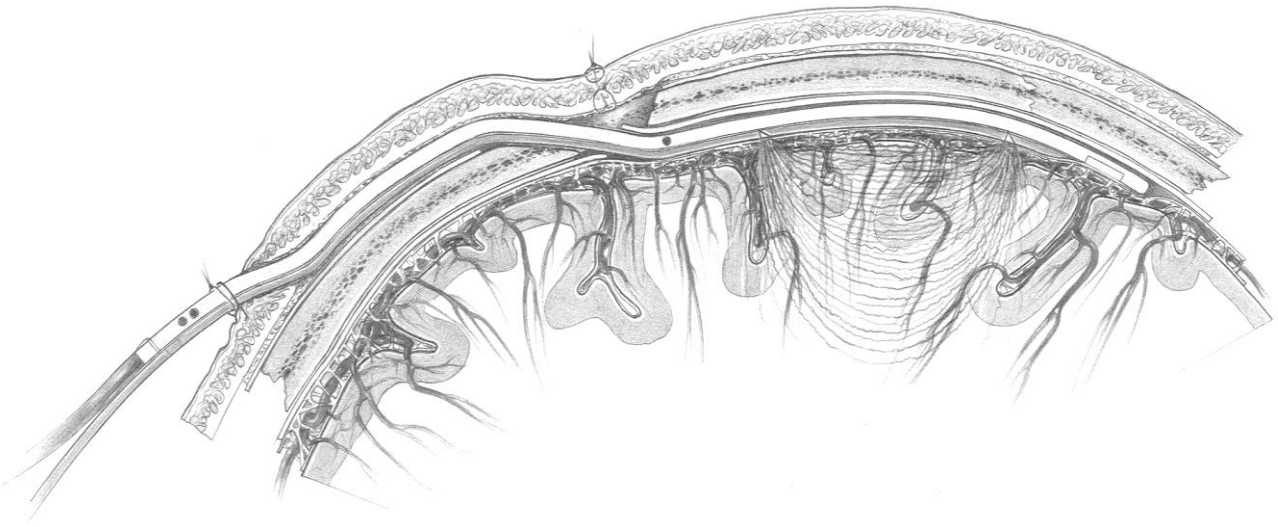

Figure 1: